33rd Annual International Conference of the IEEE EMBS
Boston, Massachusetts USA, August 30 - September 3, 2011

Theoretical Framework for Estimating the Conductivity Map of the Retina through Finite Element Analysis

Bahman Tahayori[1,*], *Member, IEEE*, Hamish Meffin[1,3], Nicholas A. Venables[1],
David B. Grayden[1,2,3], *Member, IEEE*, Anthony N. Burkitt[1,2,3], *Senior Member, IEEE*

***Abstract*— A mathematical framework for estimation of the conductivity map of the retina is presented. The problem is formulated and solved in two-dimensional space considering hypothetical inhomogeneity in the conductivity profile at each layer of the retina in x and y directions. Finite element analysis is used to solve the equation of continuity in steady state to simulate voltage measurements as well as estimate the conductivity map. The results of simulated noisy data for an inhomogeneous retina layer and the fovea, which has a more complicated geometry, are presented. The error study of the estimated conductivity map shows that the error for an inhomogeneous conductivity profile is approximately 2% and the error for calculating the fovea conductivity map is just above 8%. This method can be extended to three-dimensions and can also be used to measure the impedance of different layers of the retina for alternating currents.**

I. INTRODUCTION

Vision restoration for people suffering from Retinitis Pigmentosa (RP) and Age-related Macular Degeneration (AMD) may be achieved by using visual neuro-prosthesis devices [1], [2]. In these types of devices, the retina is electrically stimulated to generate a spot of light in a patient's visual field referred to as a *phosphene* [3].

The conductivity (σ) of the retina at different layers is important in designing an optimal stimulation pattern as well as optimisation of the electrode geometry, such as diameter, penetration depth, and pitch factor. In general, the retina conductivity profile depends on location as well as direction of measurements, meaning that the retina is inhomogeneous and anisotropic [4]. Inhomogeneity and anisotropy of the retinal tissue raise difficulties when attempting to measure the conductivity of the retina.

The electrical conductivity variations within the retinas of different animal species have been explored through experiments. Karwoski *et al.* [4] have detailed how the resistance of the retinal layers of a frog vary. In [5], the Current Source-Density (CSD) method is used to determine the resistivity profile of a New-Zealand White Rabbit retina.

While resistivity depth profiles of retinas have been obtained through experiments previously, they have been solved for under the assumption that the retina is comprised of layers that are homogeneous within themselves [6], [7].

Kasi *et al.* [8] have developed a technique for measuring the resistivity map of a retina using bipolar microelectrodes. They have employed the peak resistivity frequency method to find the resistivity map of rat and embryonic chick retinas. Microelectrodes provide more localised and stable measurements compared to the classical methods. Moreover, the experimental setup is simpler in this case.

The objective of this paper is to design a mathematical framework to calculate the conductivity of retina based on discrete measurements of voltage in the tissue. As there is no gold-standard measurement available for conductivity map and associated voltages, we generate the synthetic data based on a given conductivity profile to be able to measure the performance of the proposed method quantitatively. To this end, the equation of continuity [9] is expanded in Cartesian coordinates and is solved subsequently to simulate a voltage map on an object. In the second step, the simulated data and their partial derivatives are used as the coefficients of the equation of continuity to estimate the conductivity map of the object.

In Section II, the theory of the problem and the two key steps in our approach are formulated. Simulation results for an inhomogeneous tissue and fovea with a more complicated geometry that, to the best of our knowledge, have not been addressed previously are presented in Section III. The parameters affecting the outcome of the method and practical issues associated with the problem are addressed in Section IV. Conclusions and future avenues for extension of this work are described in Section V.

II. THEORY

Consider a tissue which can be represented by a connected set $\Omega \subset \mathbb{R}^n$, where n is an integer representing the spatial dimension. The equation of continuity in steady state for this object is represented by

$$\nabla \cdot (\sigma(\mathbf{r}) \nabla v(\mathbf{r})) = 0, \qquad \mathbf{r} \in \Omega, \tag{1}$$

with proper boundary conditions on the surface of the tissue, $\partial\Omega$.

In order to investigate the accuracy of the method developed here, we first assume that the conductivity map is given and then simulate the voltage map, $v(\mathbf{r})$, based on Equation (1). In the second step, Equation (1) is solved for $\sigma(\mathbf{r})$ using the voltage map calculated in first step. We refer to the first step as the *forward problem* and the second step as the *backward problem* throughout.

The procedures of the forward and backward problems are represented in Figure 1. As shown in Figure 1(a), the geometry and boundary conditions are determined based on the given conductivity map to set-up the problem. For

[1] Department of Electrical and Electronic Engineering, The University of Melbourne. [2] Bionics Institute. [3] NICTA Victoria Research Labs. *Corresponding author, bahmant@unimelb.edu.au.

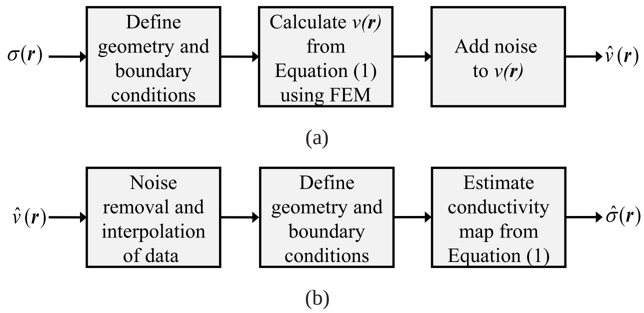

Fig. 1. The steps of the forward and backward problem.

nontrivial cases, where a closed form solution to Equation (1) does not exist, the Finite Element Method (FEM) is adopted to calculate the voltage map, $v(\mathbf{r})$, on the tissue, Ω, numerically. In practice, noise exists in all measurements, thus we consider additive noise in our simulations to give the noisy voltage map, $\hat{v}(\mathbf{r})$.

The steps for solving the backward problem, which in practice is the main problem to be solved, are shown in Figure 1(b). The first step in finding the conductivity map is to remove noise from the data. The cleaned data can be interpolated to make the voltage data smooth over a grid that can be used to solve the partial differential equation. To find the conductivity map, the geometry should be defined as similarly as possible to geometry of the tissue. After setting boundary conditions, the coefficients of Equation (1) are calculated numerically and this equation is solved by FEM to determine an estimate of the conductivity map, $\hat{\sigma}(\mathbf{r})$.

The main objective in solving the problem is to minimise the difference between the estimated map and the original one. In this paper, without loss of generality, we formulate and solve the forward problem as well as the backward problem in two-dimensional space, $n = 2$.

A. Forward Problem Formulation

The objective in the forward problem is to calculate the voltage values on the object given the conductivity map, $\sigma(x, y)$. Equation (1), which is the main equation governing the relationship between voltage and conductivity can be expanded in Cartesian coordinates, which results in

$$\sigma(x,y)\left(\frac{\partial^2 v}{\partial x^2}+\frac{\partial^2 v}{\partial y^2}\right)+\frac{\partial \sigma(x,y)}{\partial x}\frac{\partial v}{\partial x}+\frac{\partial \sigma(x,y)}{\partial y}\frac{\partial v}{\partial y}=0, \tag{2}$$

with the boundary conditions

$$\begin{aligned} &v(y=y_0)=0, \quad v(y=y_1)=V_0,\\ &\left.\frac{\partial v}{\partial x}\right|_{x=x_0}=0, \quad \left.\frac{\partial v}{\partial x}\right|_{x=x_1}=0. \end{aligned} \tag{3}$$

Equation (2), which is a second order linear Partial Differential Equation (PDE) in terms of the dependent variable v, is solved to find the voltage map on the tissue.

B. Backward Problem Formulation

In the backward problem, the conductivity map is unknown and is estimated from the given voltage map and proper boundary conditions. The results obtained from the forward problem are used as the input in this case. Equation (2) may be rewritten in the following form

$$a(x,y)\frac{\partial \hat{\sigma}}{\partial x}+b(x,y)\frac{\partial \hat{\sigma}}{\partial y}+c(x,y)\hat{\sigma}(x,y)=0, \tag{4}$$

with the boundary conditions

$$\hat{\sigma}(x_0,y)=\sigma_{x_0}, \qquad \hat{\sigma}(x,y=y0)=\sigma_{y_0}, \tag{5}$$

where

$$a(x,y)=\frac{\partial \hat{v}(x,y)}{\partial x}, \tag{6a}$$

$$b(x,y)=\frac{\partial \hat{v}(x,y)}{\partial y}, \tag{6b}$$

$$c(x,y)=\frac{\partial^2 \hat{v}(x,y)}{\partial x^2}+\frac{\partial^2 \hat{v}(x,y)}{\partial y^2}, \tag{6c}$$

in which $\hat{v}(x, y)$ represents the noisy voltage values and $\hat{\sigma}$ is an estimate of the original conductivity map to be determined. Equation (4) represents a first order linear PDE [10], [11]. It is worth mentioning that when the coefficients of Equation (4) are discontinuous, the error of numerical solutions to the problem can be unpredictably large [12].

C. Simulation Methods

Simulation of the forward and backward problems is conducted in finite element analysis software, COMSOL 4.1. In our simulations, we consider a Gaussian distribution for the additive noise such that the resultant Signal-to-Noise Ratio (SNR) is 20dB. In simulating the voltage map for the forward problem, the *Electric Current (ec)* model in the *AC/DC* module is selected. The *Coefficient Form PDE (c)* model in the *Mathematics* module is adopted to solve the backward problem. Since no dynamics is involved in the backward or forward problems, *stationary* study type is chosen to solve the relevant partial differential equations. In both cases, COMSOL internal analytic functions are used to define the geometry as well as the desired conductivity map.

In solving the backward problem, a two-dimensional interpolation function is adopted to introduce coefficients of Equation (4) in matrix form to COMSOL. In all simulations, *Direct PARDISO* with its default parameters is used.

III. SIMULATION RESULTS

In order to test the performance of the proposed method, we simulate the equation of continuity for an inhomogeneous conductivity and a nontrivial geometry.

A. Example 1: Inhomogeneous Layer

We first consider the case of a single inhomogeneous layer. We assume the conductivity inside the layer varies in both the x and y directions. Since conductivity does not alter abruptly inside a layer, we consider a conductivity map of the form

$$\sigma(x,y)=1+0.1(\sin 5\times 10^4 x+\sin 10^5 y), \tag{7}$$

which changes considerably in two-dimensions as represented in Figure 2. The objective is to estimate $\sigma(x, y)$ using the method described in Section II. To this end, we apply a constant electric field in the y direction with $V_0 = 1$V and we assume that the sides of the geometry are insulated. The noisy voltage map generated by solving the forward problem is shown in Figure 3. The estimated conductivity map through solving Equation (4) is represented in Figure 4. The maximum error of the solution is below 2% as shown in Figure 5.

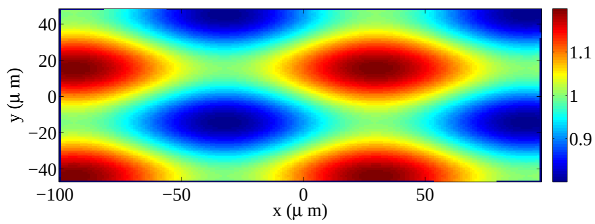

Fig. 2. The given inhomogeneous conductivity map described by Equation (7). We assume that tissue size is 200μm$\times 100\mu$m. The color map indicates the magnitude of the conductivity.

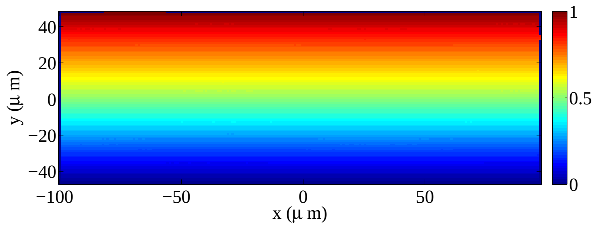

Fig. 3. The voltage conductivity map across the object shown in Figure 2. A constant field is applied in the y direction with V(y = -100μm)=0 and V(y = -100μm)=V_0=1V. The sides of the geometry at $x = \pm 100\mu$m are considered to be insulated. The color map represents the voltage magnitude at each point.

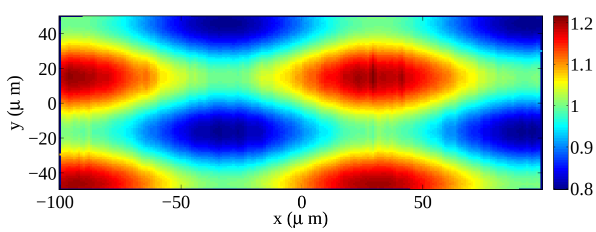

Fig. 4. The estimated conductivity map for Example 1 calculated by solving the backward problem. The color map indicates the magnitude of the estimated conductivity at different points.

B. Example 2: Fovea

We now solve the problem for a typical fovea, which has a more complicated geometry. We consider one layer of fovea with $\sigma_f = 0.5$S/m in our simulations that can be extended to more layers. We approximate the geometry of the fovea with a Gaussian function and we assume that the tissue is surrounded by saline with $\sigma_s = 2$S/m, which will be used as the boundary conditions. The given conductivity map and the resultant voltage map are shown in Figures 6 and 7, respectively. The estimated conductivity map and the error of calculation in the presence of noise are represented by Figures 8 and 9, respectively. The maximum error of the conductivity map estimation in this case is approximately 8% which is larger than the error of Example 1.

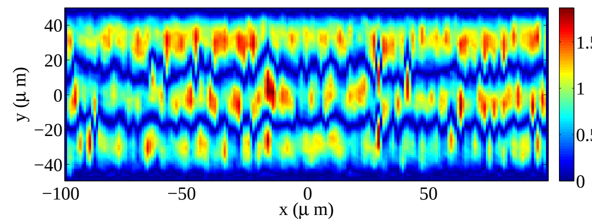

Fig. 5. The percentage error between the estimated conductivity map calculated by solving Equation (4) and the given conductivity map in Example 1.

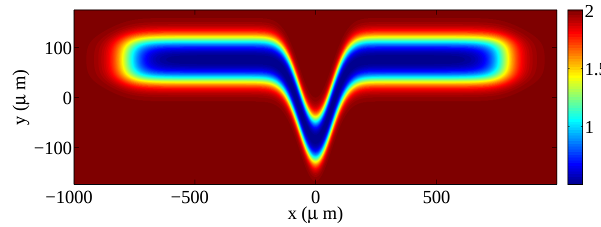

Fig. 6. The conductivity map of a one layer fovea with maximum $\sigma_f = 0.5$S/m presented in Example 2. The geometry of fovea is approximated by a Gaussian function and it is assumed that the tissue is located in saline with $\sigma_s = 2$S/m.

IV. DISCUSSION

The results presented in this paper clearly show that the proposed theoretical framework generates a potentially satisfactory conductivity map for given noisy voltage measurements. However, it should be noted that we have assumed the electrode tissue impedance [8], [13] and the electrode tissue gap [14] is the same at all points and therefore could be neglected in our calculations. Other important practical issues are the damage caused by each electrode to the retina and the relative movement between the electrode and the tissue at the time of measurement, which can affect the

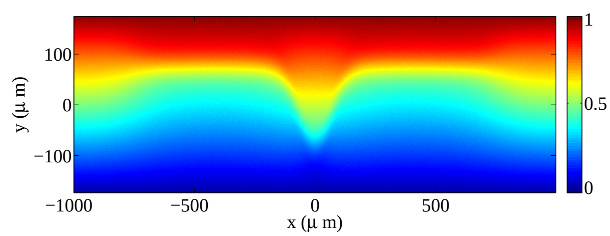

Fig. 7. The voltage conductivity map across the fovea represented by Figure 6. A constant field is applied in the y direction with V(y = -150μm)=0 and V(y = 150μm)=V_0=1V. The sides of the geometry at $x = \pm 1000\mu$m are considered to be insulated. The color map represents the voltage magnitude at each point.

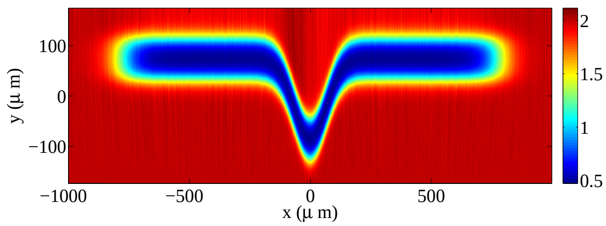

Fig. 8. The estimated conductivity map of the fovea presented in Example 2. The calculated map is found by solving the backward problem.

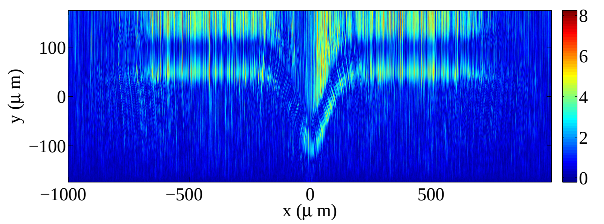

Fig. 9. The percentage error between the estimated conductivity map of the fovea calculated by solving Equation (4) and the given conductivity map in Example 2.

results unpredictably.

A. Effect of Noise on Estimated Conductivity Map

Because first and second derivatives are used to solve the conductivity map when the tissue is considered to be inhomogeneous or when it has a complicated geometry, it is expected that the accuracy of the method increases considerably along with the increase in SNR of measurements. The simulations for the examples presented in Section III have been repeated for different values of SNR. Figure 10 shows the maximum error at different SNR values in the conductivity map calculation, which infers that at low SNRs the error is very high as expected. Moreover, it is obvious that error in estimating the conductivity map of fovea is higher than the inhomogeneous case.

V. CONCLUSIONS

In this paper, a theoretical framework for calculating the conductivity map of the retina was developed. The inhomogeneity of the tissue in two-dimension as well as a complicated geometry were taken into account and it was shown that through finite element analysis, estimating the conductivity map of the retina with small error is achievable. Since inhomogeneity of retina affects the outcome of electrical stimulation of neural tissue, the method developed here can help researchers to design optimal stimulation patterns that can improve the quality of visual prostheses.

The method presented here will be extended to three dimensions and anisotropy of the tissue will be taken into account as well. Moreover, the problem will be revisited for sinusoidal stimulations that leads to calculation of the retina impedance at different frequencies which is an active area of research.

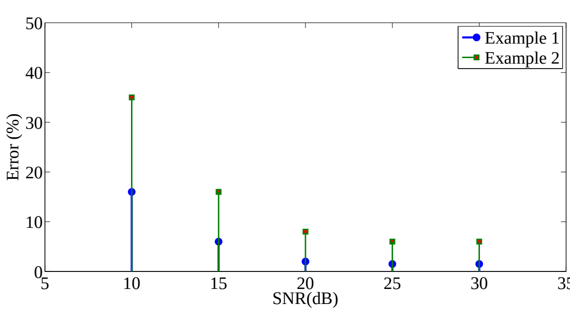

Fig. 10. The percentage error in estimation of the conductivity map versus SNR of voltage measurements for the examples presented in Section III.

VI. ACKNOWLEDGMENTS

This research was supported by the Australian Research Council (ARC) through its Special Research Initiative (SRI) in Bionic Vision Science and Technology grant to Bionic Vision Australia (BVA). The Bionic Ear Institute acknowledges the support it receives from the Victorian Government through its Operational Infrastructure Support Program.

REFERENCES

[1] J. Tombran-Tink, C. J. Barnstable, and Joseph, Eds., *Visual Prosthesis and Ophthalmic Devices - New Hope in Sight*, ser. Ophthalmology Research. Humana Press, 2007, vol. XII.

[2] D. Palanker, A. Vankov, P. Huie, and S. Baccus, “Design of a high-resolution optoelectronic retinal prosthesis,” *Journal of Neural Engineering*, vol. 2, no. 1, p. S105, 2005.

[3] J. ao C. Martins and L. Sousa, *Bioelectronic Vision: Retina Models, Evaluation Metrics and System Design*. Bioengineering & Biomedical Engineering Series, Vol.3, World Scientific, January 2009.

[4] C. J. Karwoski, D. A. Frambach, and L. M. Proenza, “Laminar profile of resistivity in frog retina.” *J Neurophysiology*, vol. 54, no. 6, pp. 1607–19, 1985.

[5] C. J. Karwoski and X. Xu, “Current-source density analysis of light-evoked field potentials in rabbit retina,” *Visual Neuroscience*, vol. 16, pp. 369–377, 1999.

[6] H. Heynen and D. Norren, “Origin of the electroretinogram in the intact macaque eye–i. current source-density analysis,” *Vision Res.*, vol. 25, no. 5, pp. 697–707, 1985.

[7] ——, “Origin of the electroretinogram in the intact macaque eye–ii. current source-density analysis,” *Vision Res.*, vol. 25, no. 5, pp. 709–715, 1985.

[8] H. Kasi, R. Meissner, A. Babalian, H. van Lintel, A. Bertsch, and P. Renaud, “Direct localised measurement of electrical resistivity profile in rat and embryonic chick retinas using a microprobe,” *Journal of Electrical Bioimpedance*, vol. 1, pp. 84–92, 2010.

[9] D. Cheng, *Field and Wave Electromagnetics*, 2nd ed. Addison Wesley, 1989.

[10] H. Rhee, R. Aris, and N. Amandson, *First-order Partial Differential Equations: Theory and application of single equation*. Prentice Hall, April 1986.

[11] A. Polyanin, *Handbook of Linear Partial Differential Equations for Engineers and Scientists*. Chapman and Hall/CRC, 2002.

[12] L. de Simon and G. Torelli, “First order linear partial differential equations with discontinuous coefficients.” *Annali di Matematica Pura ed Applicata*, vol. 128, no. 1, pp. 325–340, 1981.

[13] S. Shah, A. Hines, D. Zhou, R. J. Greenberg, M. S. Humayun, and J. D. Weiland, “Electrical properties of retinal-electrode interface,” *Journal of Neural Engineering*, vol. 4, no. 1, p. S24, 2007.

[14] H. Kasi, A. Bertsch, J. Guyomard, B. Kolomiets, S. Picaud, M. Pelizzone, and P. Renaud, “Simulations to study spatial extent of stimulation and effect of electrode-tissue gap in subretinal implants,” *Medical Engineering & Physics*, vol. In Press, Corrected Proof, 2011.